REMARKS/ARGUMENTS

In response to the Office Action of October 21, 2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Status/Support for Amendments

Claims 1, 39,40 and 44-46 have been amended. Claims 2-38 were cancelled in a previous response (filed on July 15, 2003). Claims 39-43 are withdrawn from consideration. It is understood that claims 39-43, drawn to the non-elected invention, will remain pending, albeit withdrawn from prosecution on the merits at this time. If the examined claims of the Group I invention are deemed to be allowable, rejoinder of the remaining claims (39-43) in accordance with the decision in *In re Ochiai* is respectfully requested; since the remaining claims (39-43) are limited to the use of the biopolymer markers of claim 1.

Claims 1 and 44-46 are currently under examination. Claims 1 and 39-46 remain pending in the instant application.

No new matter has been added by the amendments to the specification made herein.

The title of the invention has been amended to correct an error in punctuation (Alzheimer's replaced Alzheimers).

In the "Background of the Invention" section a punctuation error was corrected at page 1, line 23.

The description of the reference at page 5 has been amended to correct a typographical error in the international application number. The corresponding international publication number has also been added.

The "Description of the Figures" section has been amended to add sequence identification numbers, clearly indicate that Figure 2 shows the mass spectrum profiles of the disclosed biopolymer markers, and to correct an error in punctuation (Alzheimer's replaced Alzheimers).

Several protocols at pages 41-44 have been amended to properly identify trademark names (TRITON, TRIS and EPPENDORF). The protocol titles at page 41 (lines 4 and 18), page 42 (line 10) and page 43 (lines 1 and 14) were underlined in the original disclosure and do not indicate text amended herein.

The paragraph beginning at page 46 was amended for consistency of language and to correct errors in punctuation.

In the "Detailed Description" section, the term "cerebrospinal fluid" has been added to define the abbreviation "CSF" at page 49, line 8 in order to provide additional support for cerebrospinal fluid as recited in claim 41. "CSF" is a well known abbreviation for cerebrospinal fluid in the biochemical art. Kits for

determining the presence of the claimed biopolymer markers are discussed at page 47, lines 6-23; cerebrospinal fluid is noted to be one type of sample which can be used in the discussed kits. A typographical error within the same paragraph has also been amended (skill replaced skilled).

The abstract has been amended to remove the legal phraseology, "said".

No new matter has been added by the amendments to the claims made herein.

Claim 1 has been amended to explicitly claim the biopolymer markers (SEQ ID NOS:1-4). The term "biopolymer marker" is used throughout the specification as originally filed, see, for example, page 1, line 8. Claim 1 was also amended to clarify that the claimed biopolymer markers are "isolated" and thus separated from their original environment (see the instant specification at page 20, lines 9-16).

Claim 39 has been amended to clearly disclose the relationship between the presence of the claimed biopolymer markers (SEQ ID NOS:1-4) and Alzheimer's disease. Claim 39 has also been amended to explicitly indicate how the presence of the claimed biopolymer markers are determined from mass spectrum profiles. The changes to claim 39 find basis throughout the specification as originally filed, see, for example, page 35, lines 14-18, page 46, lines 2-10

and Figures 1 and 2.

Claim 40 has been amended to provide proper antecedent basis for the term "sample".

Claim 44 has been amended to correspond with the biopolymer markers of claim 1 (as amended herein). Support for various types of kits can be found in the original disclosure, see for example, page 36, lines 9-12 and page 47, line 6 to page 48, line 15.

Claims 45 and 46 have been amended to provide proper antecedent basis for the term "kit" in claim 44 (as amended herein).

Oath/Declaration

A new declaration, which has been properly executed and dated, is filed herewith because while the original oath filed on February 12, 2002 contains the signature of Dr. John Marshall (inventor 2), the date of signature was omitted.

Restriction

The Examiner has withdrawn claims 39-43 from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention.

Request for Rejoining of Claims

Considering that claims 39-43 are limited to the use of the isolated biopolymer markers SEQ ID NOS:1-4, a search of these claims would encompass these specific biopolymer markers. The instant application is related in claim format to several other applications, both pending and issued, of which serial number 09/846,352 is exemplary. In an effort to maintain equivalent scope in all of these applications, Applicants respectfully request that the Examiner consider rejoining claims 39-43 in the instant application, which are currently drawn to non-elected inventions, under the decision in *In re Ochiai* (MPEP 2116.01) with claims (claims 1 and 44-46) of the elected invention, upon the Examiner's determination that the claims of the elected invention are allowable and in light of the overlapping search. If the biopolymer markers SEQ ID NOS:1-4 are found to be novel, methods and kits limited to their use should also be found novel.

Rejection under 35 USC 112, first paragraph

Claims 1 and 44-46, as presented on July 15, 2003, remain rejected under 35 USC 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention.

Applicants respectfully disagree with the Examiner's position.

Although Applicants believe that the instant specification, as originally filed, fully supports the claim that an isolated biopolymer marker selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4 is diagnostic for Alzheimer's disease, in the interest of compact, efficient prosecution, Applicants have removed the term "diagnostic" from the claims and note that an isolated biopolymer marker selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4 is linked to Alzheimer's disease.

According to the web site, dictionary.com, the term "linked" refers to the condition of being associated with or connected to (see attached document as accessed from the internet; reference 1). The instant specification fully supports a connection and/or an association of the claimed peptides with Alzheimer's disease. The instant specification states at page 35, lines 14-18 that an objective of the invention is to evaluate samples containing a plurality of biopolymers for the presence of disease specific biopolymer marker sequences which evidence a link to at least one specific disease state.

The "test of enablement" is whether one reasonably skilled in the art could make or use the invention from the disclosures in the

patent coupled with information known in the prior art without undue experimentation (see MPEP 2164.01).

Furthermore, the decision in *In re Brandstadter* (179 USPQ 286; MPEP 2164.05) has established that the evidence provided by applicant (to overcome an enablement rejection) need not be conclusive but merely convincing to one of skill in the art.

Applicants respectfully submit that the instant specification provides sufficient evidence to convince one of skill in the art that the claimed peptides (SEQ ID NOS:1-4) are linked and/or associated with Alzheimer's disease.

Claim 1 has been amended to specifically recite an isolated biopolymer marker selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4; peptides that the instant specification identifies as linked to Alzheimer's disease.

Claim 1, as amended herein, does not recite that the claimed isolated peptides are diagnostic for Alzheimer's disease, nor does it recite that the claimed isolated peptides are related to Alzheimer's disease, even though Applicants believe that the specification, as originally filed, fully supports both of these recitations. Furthermore, the phrase "consisting of" is closed language and excludes any element, step or ingredient not specified in the claims (see MPEP 2111.03). Thus, the scope of claim 1 is limited to these specific peptides (SEQ ID NOS:1-4).

The gel shown in Figure 1 demonstrates that the expression of the peptides represented by Band #1 differs in the disease state (Alzheimer's disease) as compared to the expression in a "normal" physiological state (age-matched or normal human serum). Thus, a difference is seen between comparable samples, suggesting that the differentially expressed peptides are linked to the disease state (Alzheimer's disease).

The specification, as originally filed, does provide a precise protocol on how to analyze the data obtained from the disclosed method. Page 25, line 16 to page 26, line 2 of the instant specification discloses a general outline of how to carry out the disclosed methods. Page 26, lines 6-13 of the instant specification further describes how samples were compared to develop data and indicates how biopolymer marker peptides were selected as notable sequences. This passage of the instant specification also discloses how certain peptides were selected from a plurality of molecules found within a sample and how peptides were deemed evidentiary of a disease state. Page 5, lines 12-20 also describes how biopolymer markers are evaluated according to the methods of the instant invention. Page 46, lines 18-20 of the instant specification clearly states the steps of the invention include obtaining a sample from a patient and conducting an MS analysis (mass spectrometry) on the sample. Mass spectrometry is commonly

practiced and one of skill in the art would know how to analyze and obtain information from mass spectrometry profiles. It is clear that the data presented in the instant specification was obtained by carrying out mass spectrometry. Thus, Applicants assert that the specification, as originally filed, provides a precise protocol on how to analyze the data obtained by the disclosed protocol.

Additionally, Applicants respectfully submit that such protocols are common practice in the field of proteomics.

For example, Scott D. Patterson presents the state of the art in mass spectrometry/proteomics by summarizing the Asilomar Conference on Mass Spectrometry (see attached article Physiological Genomics 2:59-65 2000; reference 2). This conference took place in 2000, thus coinciding with the time that the instant inventors were working to develop the instant invention.

In the disclosed method of the instant invention, proteins (as seen on a gel) that are identified as differentially expressed between a disease and a non-disease state are selected for excision (from the gel) and identification (see, for example, page 38, lines 5-9 of the instant specification as originally filed, and Figure 1). Such selection methods are common practice in the search for biomarkers of specific physiological states. For example, at page 61, right column of Patterson, several automation processes are discussed in the section titled "Automated identification of gel-

separated proteins by mass spectrometry". This discussion begins with the following statement:

"Following quantitative analysis of 2-DE patterns, the next step is the identification of all protein spots that display differential expression."

Thus, it is concluded that it is common practice to select potential disease markers by their differential expression between a disease and a non-disease state.

Furthermore, Applicants respectfully submit that many of the methods disclosed in the instant specification are routinely practiced by those of ordinary skill in the art also attempting to identify biomarkers of particular physiological states.

For example, at page 64, left column of Patterson is a description of the SELDI approach (as discussed at the conference by Scot Weinberger) wherein defined chemical/biochemical surfaces are utilized to allow fractionation of proteins from biological fluids in a reproducible manner. This reproducibility allows comparisons between different samples to be made. Weinberger described a search for markers of benign prostate hyperplasia that, like prostate cancer, displays elevated prostate specific antigen (PSA) levels. The fraction exhibiting a difference between these samples was able to be enzymatically digested, and a number of peptides were generated. These peptides were able to be fragmented

using the MALDI-Qq-TOF (a procedure described by Ken Standing at the conference, page 62, left column of Patterson). It was found that there appears to be a difference in the relative level of seminogelin fragments between these two states (prostate cancer and benign prostatic hyperplasia), thus providing a potential differential marker.

Applicants respectfully draw the Examiner's attention to the fact that the method described by Weinberger is analogous to the method described in the instant specification. Furthermore, when interpreting data Weinberger uses the same approach to interpretation as the instant inventors in order to identify seminogelin fragments as a potential marker to distinguish between benign prostate hyperplasia and prostate cancer based on differential expression of the fragments. Additionally, Applicants respectfully point out to the Examiner that Weinberger linked differential expression of seminogelin to benign prostate hyperplasia and prostate cancer without statistical analysis or analysis of a sample from a control patient free of disease or analysis of a sample from a patient having another disease, which is not benign prostate hyperplasia or prostate cancer. Such linking of markers with disease through differential expression is commonly practiced in proteomics.

Furthermore, Applicants assert that those of skill in the art

are both highly knowledgeable and skilled and it is obvious that no undue experimentation would be required for a skilled artisan to follow any of the electrophoretic, chromatographic and mass spectrometric protocols presented in the instant specification in order to use the claimed invention. One of skill in the art would be able to view a gel, such as that shown in Figure 1 from which the claimed peptides were identified (SEQ ID NOS:1-4), and recognize a difference between two comparable samples (disease state vs. non-disease state) and further recognize that the peptides present within the gel are differentially expressed between the two sample types.

The exemplary preparatory protocols which can be used to carry out the methods of the invention clearly indicate that the samples used are samples of sera, for example, see step 3 of the DEAE column protocol at page 41. However, other body fluids and/or tissues can also be used, see page 47, lines 19-23. These samples are obtained from a human patient, see page 46, lines 18-20 of the instant specification. The lanes of the gel shown in Figure 1 are clearly labeled with patient numbers that indicate if the sample shown in each lane is obtained from an Alzheimer's patient (lane 1, AD-H-S-004, for example), a patient age matched with an Alzheimer's patient (lane 6, AG-AD-H-S-003, for example) or a sample pooled from a plurality of normal patients (lane 9, pooled

NHS). The data presented in Figure 1, derived from the working examples, discloses that the claimed peptides (SEQ ID NOS:1-4)are differentially expressed between Alzheimer's disease and a physiological state age matched with Alzheimer's disease, thus it can be reasonably predicted that such peptides are linked to Alzheimer's disease.

Thus, based upon the above comments, Applicants contend that a skilled practitioner would find that the data presented in the instant specification is convincing with regard to a link between the claimed biopolymer marker peptides (SEQ ID NOS:1-4) and Alzheimer's disease.

Considering the above comments, it is clear that both the specification and the prior art disclose how to make and use the instant invention. Accordingly, Applicants respectfully contend that the instant invention satisfies the "test for enablement" since one skilled in the art could make or use the invention from the disclosures in the specification coupled with information known in the prior art without undue experimentation.

The Examiner is reminded that all questions of enablement should be evaluated against the claimed subject matter and the focus of the examination inquiry should be a question of whether everything within the scope of the claims is enabled (see MPEP 2164.08).

Accordingly, an Applicant is not required to enable material which is not claimed. The pending claims do not recite that the claimed peptides are diagnostic for any pathological condition, including Alzheimer's disease. Thus, no teachings regarding diagnostics are necessary in order to provide evidence for enablement of the pending claims. However, even if the pending claims were drawn to diagnostics, Applicants respectfully submit that such claims would be enabled without analysis of a sample from a control patient free of disease or analysis of a sample from a patient having another pathological condition; since, linking of markers with a disease by differential expression of peptides alone is commonly practiced (see above discussion of the Weinburger study).

Additionally, Applicants assert that the intended purpose of the invention is to provide improved, alternative means for diagnosis of Alzheimer's disease which can easily be performed by an untrained individual without the need for additional testing. If "follow-up" diagnostic methods are required, then the diagnostic process is lengthened and the invention fails to fulfill its intended purpose.

The guidelines for a "test of enablement" indicate that if a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard

modes of administration are known and contemplated, 35 USC 112, is satisfied (see MPEP 2164.01(c)).

Applicants assert that SEQ ID NOS:1-4 are linked to Alzheimer's disease, however, do not claim that such sequences are unique markers for any particular disease or condition.

Although the prior art does not specifically recognize that the claimed markers, fragments of fibronectin identified as SEQ ID NOS:1-4, are related to Alzheimer's disease, it does recognize that basement membrane components such as fibronectin have been implicated in the genesis of amyloid proteins. Thus, basement membrane components such as fibronectin potentially contribute to the pathologic amyloidogenic process in Alzheimer's disease (see attached abstract of Narindrasorasak et al. Laboratory Investigation 72(3):272-282 1995; reference 3). Considering this knowledge, when one of skill in the art observes differential expression of the claimed peptides between Alzheimer's disease and an age-matched normal physiological state; one of skill in the art will connect these peptides with potential diagnostics and/or therapeutics for Alzheimer's disease.

Thus, Applicants respectfully submit that since the specification demonstrates a link between the claimed peptides (SEQ ID NOS:1-4) and Alzheimer's disease and that this link connotes the use of the claimed peptides in potential diagnostics and/or

therapeutics of Alzheimer's disease, the requirement of "how to use" under 35 USC 122, first paragraph is satisfied.

Furthermore, Applicants respectfully submit that one of ordinary skill in the art would find the suggestion of a link between the claimed peptides (SEQ ID NOS:1-4) and Alzheimer's disease to be reasonable.

At page 46, of the instant specification as originally filed, SEQ ID NOS:1-4 are identified as fragments of the fibronectin precursor protein. Fibronectin is an extracellular matrix protein found in most animal tissues (see attached definition of fibronectin as accessed from the internet at the Ergito Life Sciences glossary; reference 4) and has been implicated in the genesis of amyloid proteins. Thus, fibronectin potentially contributes to the pathologic amyloidogenic process in Alzheimer's disease (see attached abstract of Narindrasorasak et al. Laboratory Investigation 72(3):272-282 1995; reference 3). One of skill in the art, considering that fibronectin has been shown to contribute to the pathogenesis of Alzheimer's disease by interaction with amyloid proteins, upon observation of the differential expression of the claimed peptides in Alzheimer's disease versus an age-matched physiological state determined to be normal with regard to Alzheimer's disease, would find it reasonable to believe that these peptides are related to Alzheimer's disease.

Therefore, one of ordinary skill in the art would recognize the linkage between SEQ ID NOS:1-4, fibronectin and Alzheimer's disease and thus would also find the suggestion of SEQ ID NOS:1-4 as markers for Alzheimer's disease entirely reasonable.

The Examiner continues to assert that it is not clear to one of ordinary skill in the art as how to use the recited invention for a positive diagnosis of Alzheimer's disease. The Examiner asserts that applicant fails to provide the sample size for the necessary statistical analysis, i.e. patient number versus healthy control ones. It is important to reveal such information for establishing the reliability of the recited "diagnostic biomarkers" for the disease of interest. Additionally, the Examiner asserts that the current claimed invention lacks the statistical representation in a general population for a generic well-known disease and further that the sample size as shown in Figure 1 is too small to be considered statistically reliable. The Examiner concludes that simply gathering data from Figures 1 and 2, with a limited sample size, cannot serve molecular diagnostic purpose in a general population.

Applicants respectfully disagree with the Examiner's position as the Examiner apparently believes that complex statistical analysis is required to convince one of skill in the art that a peptide is linked with a disease condition.

As emphasized in the above discussion of Weinberger's study, differential expression of a peptide between a disease state and a normal physiological state is sufficient to link the differentially expressed peptide with the disease state.

Furthermore, Tockman et al. (Cancer Research Supplement 52:2711s-2718s 1992; reference 5) discuss markers for the early detection of lung cancer. Tockman et al. link several biopolymer markers to lung cancer in a manner analogous to that of the instant specification. Tockman et al. state at page 2712s, left column:

"A functional membrane-associated bombesin receptor recently has been isolated from human small cell lung carcinoma (NCI-H345) cells (23), and bombesin-like peptides have been found in the bronchial lavage fluid of asymptomatic cigarette smokers (24). Thus markers of growth factor expression, insofar as they reflect oncogene activation, may also hold promise for the detection of early (preneoplastic) lung cancer."

From this statement, it is clearly evident that Tockman et al. link bombesin with small cell lung cancer and associate it with potential diagnostics for small cell lung cancer. It does not appear that bombesin was "validated" and/or subjected to any "statistical analysis" prior to this association.

Additionally, Tockman et al. state at page 2713s, left column:

"Evidence of a transformed genome, by expression of tumor-

associated antigens, oncofetal growth factors, or specific chromosomal deletions has clear biological plausibility as a marker of preclinical lung cancer."

From this statement, it appears that Tockman et al. believe that the expression of certain proteins provides evidence of a transformed genome and since this transformed genome is associated with lung cancer, it is reasonable to believe that these certain proteins are potential markers.

Such parallel reasoning between Tockman et al. and the instant specification, further supports Applicants contention that one of ordinary skill in the art would not have any difficulty seeing a link between the claimed biopolymer marker peptides (SEQ ID NOS:1-4) and Alzheimer's disease.

It is noted that in chemical and biotechnical applications, evidence actually submitted to the FDA to obtain approval for clinical trials may be submitted to support enablement of an invention. However, considerations made by the FDA for approving clinical trials are different from those made by the PTO in determining whether a claim is enabled (see *Scott v. Finney* 32 USPQ 2d 1115 and MPEP 2164.05)

The Examiner is reminded that the considerations made by the PTO involving clinical trials are less stringent than the considerations made by the FDA. Evidence presented by applicant to

provide enablement of an invention need only be convincing to one of skill in the art and not conclusive. Thus, Applicants respectfully submit that, contrary to the Examiner's assertion, statistical analysis is not necessary in order to show that the instant invention is enabled.

In conclusion, Applicants claim that the differential expression of SEQ ID NOS:1-4 between Alzheimer's disease patients and patients determined to be normal with regard to Alzheimer's disease evidences a link between the claimed peptides (SEQ ID NOS:1-4) and Alzheimer's disease; a statement which is enabled by the instant specification, as evidenced by the arguments presented herein. Applicants assert that one of ordinary skill in the art when reviewing the instant specification, given the level of knowledge and skill in the art, would recognize the link between the claimed biopolymer markers (SEQ ID NOS:1-4) and Alzheimer's disease and would further recognize how to use the claimed peptides (SEQ ID NOS:1-4) as markers for Alzheimer's disease. Thus, Applicants respectfully request that this rejection under 35 USC 112, first paragraph now be withdrawn.

Rejection under 35 USC 102(b)

Claim 1, as presented on July 15, 2003, remains rejected under 35 USC 102(b) as allegedly being anticipated by Bernard et al.

(Biochemistry 24:2698-2704 1985).

The Examiner asserts that Bernard et al. teach isolation and characterization of human cellular fibronectin encompassing the current recited peptides of SEQ ID NOS:1 and 4 (see Figure 3). Thus, the Examiner concludes that Bernard et al. reads on and anticipates claim 1. The Examiner notes that recitation of diagnostic for Alzheimer's disease has not been given patentable weight because the recitation occurs in the preamble.

In the Response filed on July 15, 2003, Applicants contend that the Bernard et al. reference does not specifically teach the recited peptides (SEQ ID NOS:1-4) and no where does Bernard et al. teach that the specific peptides serve as a diagnostic marker for Alzheimer's disease.

The Examiner did not find Applicants' argument to be persuasive. The Examiner asserts that claim 1 is directed to peptide products and indicates that the intended use is given no patentable weight. The Examiner continues to maintain that although Bernard et al. do not specifically teach the recited peptides per se, the teachings of Bernard et al. still encompass and read on claim 1. The Examiner asserts that applicant does not refrain the recited peptides in a limited segment and the wording "biopolymer marker peptide" can be interpreted as broadly as to be anticipated by Bernard et al.

Applicants respectfully disagree with the Examiner's position and contend that, contrary to the Examiner's assertion, the recited peptides are refrained in a limited segment by use of the phrase "consisting of".

While Bernard et al. do disclose the amino acid sequence of the C-terminal region (794 amino acid residues)of human cellular fibronectin (see abstract; Figures 3 and 4); Bernard et al. do not disclose SEQ ID NOS:1-4 as claimed in the instant application.

Claim 1 is drawn to a biopolymer marker selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4. The phrase "consisting of" is considered closed language and excludes any element, step or ingredient not specified in the claim (see MPEP 2111.03). The confining language of the phrase "consisting of" was established by the decision in *Ex parte Dotter* (see MPEP 2173.05(h) and 12 USPQ 382). The use of closed language limits the scope of the claims to these specific peptides (SEQ ID NOS:1-4) and thus excludes the larger sequence of the C-terminal region of fibronectin disclosed by Bernard et al.

Accordingly, Applicants respectfully submit that claim 1, as presented herein, now distinguishes over the sequence taught by Bernard et al. and respectfully request that this rejection be withdrawn.

Rejection under 35 USC 103(a)

Claims 44-46, as presented on July 15, 2003, remain rejected under 35 USC 103(a) as allegedly being unpatentable over Bernard et al. (Biochemistry 24:2698-2704 1985) in view of Hutchens et al. (US 6,225,047).

The Examiner notes that the Bernard et al. reference has been discussed but is silent in teaching having peptides and the antibodies capable of binding to the peptides in a kit for conventional convenience, economy and reproducibility. The Examiner also notes that the Board of Patent Appeals and Interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. According to the Examiner Hutchens et al. teach immobilizing specific antibodies on the substrate in detecting ligands of interest (see Figure 14 and abstract). Therefore, the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time that the invention was made to have provided Bernard et al. with the kit containing antibodies immobilized on substrates as taught by Hutchens et al. for conventional convenience, economy and reproducibility in immunological detection of analytes.

Applicants respectfully disagree with the Examiner's determination that the claimed subject matter is obvious.

In order for an Examiner to establish a *prima facie* case of obviousness, the prior art reference or references when combined must teach or suggest all of the claim limitations (see MPEP 2142).

It was established above in the section regarding the rejection of claim 1 under 35 USC 102(b), that the prior art reference (Bernard et al.) does not teach or suggest the claimed peptides, SEQ ID NOS:1-4.

Thus, Applicants respectfully submit that the Examiner has failed to satisfy all the criteria necessary to establish a proper rejection of claims under 35 USC 103(a) and further contend that a biologist of ordinary skill in the art, having the references (Bernard et al. and Hutchens et al.) in front of him/her would not have the information and motivation necessary to arrive at Applicants' invention, i.e. kits for determining the presence of an isolated biopolymer marker selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4. Thus, it is respectfully submitted that the combination of the teachings of Bernard et al. and Hutchens et al. fails to reasonably teach or suggest to one of ordinary skill in the art the elements of Applicants' kit as specifically set forth in claims 1 and 44-46 as presented herein. Accordingly, Applicants respectfully submit that the claimed kit distinguishes over the prior art and respectfully request that this rejection under 35 USC 103(a) now be withdrawn.

CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,

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